National Organization for Rare Disorders, Inc.®

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August 18, 1999

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Dockets Management Branch
HFA-305
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Docket No. 99N-1737
Public Availability of Information on Clinical Trials for Investigational Devices Intended to Treat Serious or Life-threatening Conditions

Dear Sirs:

In response to the agency's request for comments (*FR June 22, 1999: Docket No. 99N-1737*), the National Organization for Rare Disorders (NORD) feels very strongly that information about clinical trials with investigational medical devices for serious or life-threatening diseases should be made available to the public through an accessible database of clinical trials.

NORD is a national non-profit voluntary health organization representing an estimated 20 million Americans with rare "orphan diseases." Under the *Orphan Drug Act of 1983*, a rare disease is a health condition that affects fewer than 200,000 Americans. There are more than 6,000 of these disorders according to the National Institutes of Health (NIH).

Because economic analysis of research and development (R&D) of pharmaceuticals is different from economic R&D factors affecting medical devices (including patents), orphan devices were not integrated into the *Orphan Drug Act*. Instead, FDA's *Humanitarian Device Exemption* provides incentives to promote development of medical devices for populations under 4,000 Americans.

NORD was the primary advocate for inclusion of the *Clinical Trials Database* provisions of FDAMA (P.L. 105-115), which was enacted on November 21, 1997. NORD remains convinced that FDA's primary mission should be to enhance and protect the public health. The public is not well served when drug and device manufacturers shroud development of new products in a cloak of secrecy while patients with serious and life-threatening diseases are desperately searching for clinical trials they can participate in.

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The congressionally mandated report of the *National Commission on Orphan Diseases* (DHHS 1989) found that 47 percent of biomedical researchers said they could not find a sufficient number of rare disease patients to participate in clinical trials, while 76 percent of rare disease patients said they wanted to participate in clinical trials but could not locate scientists studying their disease. The FDAMA mandated *Clinical Trials Database* is aimed at solving this serious obstacle to research progress and engendering hope in patients with hopeless diseases.

Listed below are direct responses to the *Federal Register* questions:

1. Public Health Need: There is an intense public health need for information about device investigations. Information about experimental medical devices is even more difficult to locate than information about investigational drugs. Both patients and physicians need, but do not have access to this information. Thus patients who might benefit from experimental devices may be unfairly prevented from learning about opportunities to enhance scientific knowledge and promote development of new treatments.

   Moreover, the rapid changes in modern technology may render new breakthrough treatments as "devices" rather than drugs. For example: implanted drug/device combinations, xenotransplanted tissues and organs, etc. These are products that do not technically fit either the current "drug" or "device" categories. If FDA classifies them as "devices," public knowledge of clinical trials will be even more imperative than it is today.

2. Will there be an adverse impact on device innovation if information on device investigations is required to be publicly disclosed? Firstly, we believe FDA's primary responsibility is consumer protection, not company protection. Therefore, it is FDA's responsibility to make and enforce policies that benefit the public health. Secondly, although companies often claim that secrecy is necessary to protect their products from competitors ("trade secrets"), one need only talk to a stock broker to learn which products each company is developing. Thus device companies cannot ethically claim that public secrecy is necessary while Wall Street secrecy is unnecessary.

   It is a public health disgrace that Wall Street knows the products that device companies are developing, but patients and physicians don't know. Therefore, public access to this information can be no threat to innovation as long as FDA does not release the blueprints for the device and other detailed factors that might enable a competitor to duplicate the product.

3. Other Factors: The Secretary should be sensitive to the fact that patients simply want to know, especially when they have a serious or life-threatening disease without satisfactory treatment alternatives, that a clinical trial on a drug or device for their health condition is underway, where the clinical sites are located, and how they can obtain further information that can help them decide whether they want to participate in the clinical trial. This is all they want. Patients do not want to see the design of the device, the materials it is made out of, nor its marketing plans, nor wiring blueprints. If device manufacturers understand that their real trade secrets will be protected perhaps they will be more willing to cooperate in this public health venture.

On page 33314, the Federal Register notice asks another series of questions. Listed below are NORD's answers to those questions:

1. **Is there a public health need for inclusion of device investigations within the scope of the data bank under 402 (j) of the PHS Act?**

   There is an absolute and critical need for public access to information about medical device investigations for serious and life-threatening health conditions. It is also critically important that information about pediatric devices is made available because there is a desperate need for small devices that can be used on infants and children.

2. **If there is a public health need, what category of device trials should be made publicly available and how should this category be defined? FDA's treatment IDE regulation applies only to devices for which no comparable or satisfactory alternative exists. Should a data bank for IDE's be similarly restricted? Should the trials that become part of the data bank include feasibility/pilot trials or only studies that are intended to demonstrate reasonable assurance of safety and effectiveness?**

   There is probably minimal or no need for information about "me-too" medical devices (e.g., pacemakers similar to those already on the market). Unfortunately, much of the medical device industry conducts R&D on devices that vary only slightly from those that are already commercially available. The critical need is for information about devices for untreatable (or unsatisfactorily treatable) health conditions, pediatric devices, as well as truly innovative products that are improvements over currently available devices. Limiting mandatory disclosure to the truly innovative products (when no comparable or satisfactory alternatives exist), and pediatric devices, would be in the best interest of the public health.

   We also suggest that clinical trials should be added to the database when they are in the more advanced investigational stages (the equivalent of phase III for drug trials). This is because earlier trials (while the product is in phase I or II) are more likely to fail; therefore, there is a higher risk to patients that the product will not be safe or effective. On the other hand, if a device manufacturer voluntarily asks for a product to be added to the database at an earlier stage of development, FDA should agree to do so if there are no significant safety or ethical questions.

3. **Investigational device trials have historically been smaller in numbers of subjects and numbers of investigational sites than investigational drug trials. What impact, both positive and negative, would the release of information have on these device trials, the sponsors, the investigators, the investigational sites, and the patients? Will a public data bank create pressures to increase the size of device trials or number of sites in situations where such expansion may increase risk to patients?**

   Understanding that device trials are usually small and the clinical trial sites for devices are usually limited, there are factors that FDA and manufacturers should be sensitive to. Most importantly, patients will have difficulty traveling to the sites, and they may ask for travel assistance to cover costs. We do not believe the patient community will demand more

clinical trial sites so that participation will be more convenient to them. Rather, it has been our experience that patients are pleased to know research is being pursued, but the onus is on them to get to the clinical trial site rather than expect the site to come to them. Moreover, if too many patients wish to enroll in the study, FDA should monitor a fair and equitable rationing system such as a computerized random selection process.

4. **IDE information is generally protected from public disclosure under FDA regulations. If public disclosure were voluntary, would disclosure by one sponsor put pressure on sponsors of similar investigations to disclose the existence of their studies against their better judgment? Is this in the interest of the public health?**

It is in the best interest of public health to have as many device investigations disclosed on the database as possible. If FDA decides that only the truly innovative products should be listed (not the "me-too" devices), it is reasonable to expect that all manufacturers will want their products listed lest their product gains a reputation as not being a true innovation.

5. **If disclosure is mandatory, is it likely to hamper innovations and investment in research and development? Would disclosure of these investigational device trials help or hinder research by increasing patient enrollment?**

It is impossible to believe that mandatory disclosure would hamper investment in R&D. Indeed, it is only logical to expect that disclosure will speed innovation because it will enhance patients' and physicians' expectations, speed recruitment of patients for clinical trials, enable physicians to locate clinical sites that might be appropriate for their patients, and enable investors to analyze the potential for growth of the company. Indeed it is difficult to believe that investors would have any interest in a company that is unwilling to reveal information about future products in its pipeline.

6. **Because sponsors can recover some of the costs of the device research and development under the investigational device regulations, should FDA be concerned that publicly available information concerning investigational device trials will result in undue financial pressure or incentives on the trial sponsors to add subjects to the trials without appropriate consideration of risk? Should FDA be concerned about the possibility that improper promotion and commercialization will occur as a result of a public data bank for IDE trials?**

Will there be a financial incentive to manufacturers who can recover the costs of R&D under the Investigational Device regulations? Our experience with investigational orphan drugs (for which some manufacturers are allowed to charge a fee) proves otherwise. Many health insurers will not pay for investigational treatments so many patients must pay out-of-pocket when a drug is not yet approved for marketing. Therefore, only a small number of patients will be able to pay (depending upon the cost of the device) and to afford travel to distant trial sites. Any manufacturer who believes he will be able to make large profits on an investigational device is out of touch with today's managed care health system. Instead, we would urge FDA to require that a percentage of product be reserved for needy patients who want to participate in the trial but cannot afford to do so.

Should FDA be concerned that improper promotion and commercialization will occur because of the data bank? If FDA and NIH control the wording of clinical trial information in the database, claims will be truthful and non-commercial. Similarly, FDA must maintain control over written information about the investigational product, including informed consent documents.

7. **Will public disclosure of information about device trials for products to treat serious or life-threatening diseases or conditions affect reimbursement policies of third party payers?**

Unfortunately, public disclosure of information about investigational devices will not affect reimbursement policies of private third-party payers, but it may affect government payers (Medicaid & Medicare). Since there is no federal law governing private health insurers, many reimbursement problems have plagued investigational drugs, and they will similarly affect devices. We caution the FDA and NIH, however, not to create categories of specific diagnoses for which government insurance will reimburse (e.g., right now Medicare will reimburse for certain investigational cancer drugs, but not investigational drugs for other diseases). Instead, if FDA and NIH wish to advise HCFA about Medicare/Medicaid reimbursement for investigational devices, we implore you to negotiate reimbursement for all serious and life-threatening diseases for which alternatives are not satisfactory.

8. **What other important information or issues should the agency consider?**

Other issues the agency should consider are the impact on the public health that secrecy has historically had and the implications of not making clinical trial information available to the public. The agency should define "trade secret" not as blanket secrecy, but rather protection of the plans, designs, ingredients, components, etc., of a medical device that might enable a competitor to copy the product. Public information about the location of clinical trials should clearly not be considered a trade secret, but a matter of public health.

Thank you for the opportunity to comment on this public notice.

Very truly yours,

Abbey S. Meyers
President

ASM:aa

cc: Stephen Groft, Director, NIH Office for Rare Diseases
Marlene Haffner, M.D., FDA Office for Orphan Products Development

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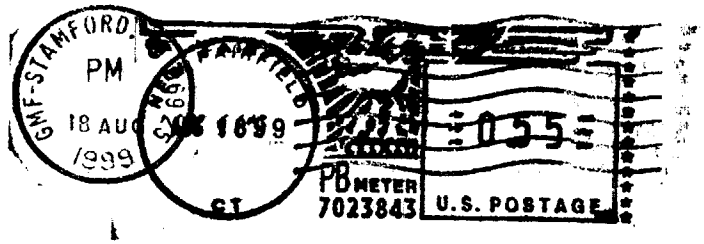

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